REMARKS

Claims 1 – 3, 6 – 11, 14 – 20, and 23 – 38 have been amended to more particularly point out and distinctly claim Applicant's inventions. In addition, corresponding amendments have been made to the specification. No new matter has been added. Before addressing the claims specifically, Applicant notes the following features of the claimed methods and apparatus. As discussed, for example, on page 1, line 19 through page 2, line 19, there is a need in the art for an automated mass spectrometry (MS) metrology in areas such as semiconductor processing. However, traditional MS apparatus requires frequent adjustment and recalibration by skilled personnel. This frequent recalibration is required to address inevitable systematic errors introduced by instrument drift and other problems. To solve this problem, Applicant has provided an automated mass spectrometry apparatus and method that relies on a ratio measurement allowing unattended and automated operation of the MS metrology tool. For example, as stated on page 10, lines 9 through 18:

In one embodiment of the invention, the method and apparatus enables the IP-MS to be operated in an unattended manner that is a substantial departure from attended operation protocol where operator calibration and analysis are typically performed. Direct comparison against a calibration curve is unnecessary through the use of ratio measurements. This is a departure from traditional instrument operation where concentrations of elements are made in comparison and where instrument drift requires frequent re-calibration required for quantitation.

Although the use of a ratio measurement eliminated the need for frequent re-calibration, that was not the only advance provided by the Applicant. In addition, Applicant enhanced the automated ratio measurement through the use of atmospheric pressure ionization (API) such as, for example, electrospray to create the ions analyzed by the mass spectrometer. Unlike the relatively harsh ionization used in traditional inductively-coupled plasma mass spectrometers , API provides a more mild ionization that preserves species information. For example, should the species Cr(III) and Cr(VI) be ionized in an inductively-coupled plasma

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MS instrument, they are ionized into the same state, namely Cr(I). A MS cannot distinguish between a Cr(I) ion that was originally Cr(III) vs. a Cr(I) ion that was originally Cr(VI). So, the species information is destroyed. However, the relatively mild ionization provided by an API ionization process would not convert Cr(III) and Cr(VI) into the same ionic form. For example, suppose a sample contains CrF_3 and CrF_6. When subjected to API, such a sample will provide $(CrF_2)+$ ions and $(CrF_5)+$ ions, thereby preserving the Cr(III) and Cr(VI) species information.

Claim 1 is directed to these beneficial features of Applicant's invention. As now recited in the preamble of claim 1, the "ratio-based" nature of the method is highlighted by the term "in-process ratio mass spectrometry." In addition, an act of "providing a spike related to the sample" is recited. Such an act is supported throughout the specification, including for example, Figures 10 and 11 and the supporting description on page 26, line 29 through page 28, line 10, which relates to the characterization of a Ni analyte using a variety of isotopically-enriched Ni spikes at differing concentrations. Given the provision of a spike and a sample, the sample may then be spiked with the spike as recited in the act of "spiking the sample with the spike and permitting equilibrium to occur therebetween" followed by an act of "subjecting said equilibrated spike and sample to atmospheric pressure ionization to create ions therefrom." Claim 1 further recites the acts of "introducing said ions into a mass spectrometer introducing said ions into a mass spectrometer for a ratio determination; and in a processor, using the ratio determination to characterize the sample." Accordingly, no new matter has been entered in claim 1.

Claims 2 – 3, 6 – 23 depend either directly or indirectly upon claim 1 and thus have been amended to share the same preamble as claim 1 and also to address a number of informalities. No new matter has been added.

Claim 24 has been amended to include all the limitations of original claim 1.

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Claim 25 has been amended analogously as discussed with respect to claim 1. Thus, no new matter has been added. Claim 25 now recites "apparatus for in-process ratio mass spectrometry comprising sample receiving apparatus adapted to receive a sample, spike introduction apparatus for introducing at least one spike into said sample for permitting equilibration therebetween, an atmospheric pressure ionizer for receiving said equilibrated sample and spike and ionizing the same, a mass spectrometer for receiving and processing said ions to form a ratio, and a processor adapted to use the ratio to characterize the analyte in the sample." Accordingly, the apparatus recited in claim 25 possesses the advantageous features of the invention described above with respect to claim 1.

Claims 26 through 38 depend either directly or indirectly upon claim 25 and thus have been amended to share the same preamble and also to address some informalities.

Claim 39 has been added. Claim 39 includes the acts recited in claim 1 and thus shares its written support and is also addressed to the same advantageous features discussed previously. However, claim 39 includes the limitation of "in effecting the equilibrium between the spike and the sample, dynamically transforming the analyte and the spike to the same species." Support for such a limitation is shown, for example, on page 9, lines 9 – 12, which states

The equilibrium between spike and sample species is achieved by dynamical pretreatment, which may be complex, oxidation, or other, of both sample and spike to transform them to the same species before pre-concentration and determination.

See also page 16, line 21 through page 17, line 27, which describes the same feature. Such a feature is very advantageous because it allows the characterization of a species without the necessity of using an isotopically-labeled spike corresponding to the same species. For example, as described on page 16, line 21 through page 17, line 27, an isotopically-labeled spike of iron nitrate could be used to characterize the amount of an iron-flouride species.

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New claim 40 depends from claim 39 and limits the dynamic transformation of the spike and sample to be a dynamic transformation of the spike.

Claim 41 has also been added and is directed to the feature of the invention discussed at, for example, page 27, line 15 through page 28, line 10. This disclosure is directed to a modification of the general automated analysis discussed with respect to claim 1. The modification is directed to an intelligent selection of spike concentration. In the example, an API-MS instrument having a conventional detection limit of 0.05 ppb is used to characterize a 0.01 ppb Ni concentration. This advance in sensitivity is provided by selecting an appropriate spike concentration as determined by the analyte concentration in the sample. Accordingly, claim 41 recites an act of "analyzing a first sample from a source having an analyte" and acts of "providing a second sample from the source; providing a spike related to the analyte, the spike having a concentration based upon the analysis of the first sample." Having thus provided a spike with the appropriate concentration, the remaining acts are analogous to those already discussed with respect to claim 1.

Applicant respectfully traverses the rejection of claims 1 through 24 as being unpatentable over claim 1 of USP 5,414,259 (the '259 patent) in view of the Fassett reference. Given the significant differences between the present claims 1 through 24 and claim 1 of USP 5,414,259, Applicant would like to provide some general background before addressing these rejections. As indicated by the title of '259 patent, this patent discloses a method of <u>speciated</u> isotope dilution mass spectrometry (SIDMS). Applicant has deliberately highlighted the word "speciated" because of the significant differences that lie behind this word and the subject matter of pending claims 1 through 24.

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To practice SIDMS, one must spike with an isotope-altered form of the specie(s) one is interested in characterizing. For example, consider Example II starting at Col. 10, line 65 of the '259 patent. In this example, the patentee was interested in characterizing the amounts

of Cr(III) and Cr(VI) within a sample. Since the patentee was employing SIDMS, he spiked the sample with known amounts of Cr(III)-50 and Cr(VI)-50. In other words, if one is interested in species "x," in an SIDMS process you must spike with an isotope-enriched form of the species x. After equilibrating the spiked sample, it was subjected to mass spectrometric analysis. As discussed in Col. 16, lines 1-7, a number of mass spectrometric instruments could be used including inductively coupled mass spectrometry (ICP-MS) and thermal ionization mass spectrometry (TIMS). Regardless of the specific instrument used, at the filing date of '259 patent (May 9, 1995) the ionization was so harsh that species information is destroyed. For example, as Cr(III) and Cr(VI) pass through an inductively-coupled plasma stage of an ICP-MS instrument, both species are converted to Cr(I). Thus, you must first separate the species such as Cr(III) and Cr(VI) from each other before their characterization in the mass spectrometer. As discussed in the '259 patent, for example, at Col. 13, line 65 through Col. 14, line 13, a number of separation techniques may be employed to separate the species including chromatography. The goal is to physically separate the species before they are introduced into the mass spectrometer. These well-known characteristics of an SIDMS process are reflected in claim 1 of the '259 patent.

Specifically, claim 1 of the '259 patent includes an act of "converting said stable isotope to a speciated enriched isotope corresponding to the species to be measured in said sample." As discussed above, this reflects the speciated nature of SIDMS – you spike with an isotope-enriched form of the species(s) you are analyzing. In addition, claim 1 of the '259 patent includes an act of "separating all said species from said sample ...." As also discussed above, species need separation before an SIDMS analysis can be completed as claimed in the '259 patent.

Now contrast these and other elements of claim 1 to those recited in pending claim 1 of the present application. Here, Applicant has claimed an in-process ratio mass spectrometry

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method. In contrast, the SIDMS method disclosed in the '259 patent is a fundamentally offline process, requiring considerable user interaction in regards, for example, to calibration. In even sharper distinction, claim 1 does not require the use of isotope-enriched forms of the species being analyzed. Instead, claim 1 recites the act of "providing a spike related to the sample." This act does not require an isotope-enriched species corresponding to the species being analyzed as required in an SIDMS process such as that disclosed in the '259 patent. Because the '259 patent was limited to a disclosure of an SIDMS technique, the Examiner further combined this patent with the Fassett reference, which discloses a thermal ionization mass spectrometric (TIMS) technique. But Fassett also requires a separation step as does the '259 patent. Specifically, on page 644, Fassett discloses an analysis of vanadium in crude oil, wherein after equilibration of the spike, "the vanadium was separated by ion exchange and the isotopic composition determined by TIMS. In sharp contrast, claim 1 needs no separation step because of the act of "subjecting said equilibrated spike and sample to atmospheric pressure ionization to create ions therefrom." Advantageously, such an act requires no separation before the ions are introduced into a mass spectrometer, thereby enhancing the automated character of Applicant's invention. Neither the '259 patent nor the Fassett reference, alone or in combination provide any teaching or suggestion for such an advantageous feature. Thus, Applicant respectfully submits that claim 1 is plainly allowable over both the '259 patent and the Fassett reference. Dependent claims 6 and 9 of the '259 patent add nothing further. Indeed, claim 9 of the '259 patent expressly limits the separation step to involve chromatography.

Because claims 2 – 3, 6 – 20, and 23 depend either directly or indirectly upon claim 1, they are patentable over the claim 1, 6, and 9 of the '259 and the Fassett reference for at least the same reasons. Because claims 4, 5, 21, and 22 have been cancelled, their rejections are mooted.

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Applicant gratefully acknowledges the previous indication that claims 25 through 38 are allowable. Applicant respectfully submits that, as amended, these claims remain allowable for the reasons discussed above. In addition, new claims 39 through 41 are allowable for at least the same reasons.

The amendments to the specification are supported analogously as discussed with respect to the claim amendments. No new matter has been added.

CONCLUSION

For the foregoing reasons, Applicant respectfully submits that pending claims 1 – 3, 6 – 20, and 23 – 39 are in condition for allowance.

If there are any questions regarding any aspect of the application, please call the undersigned at 949-752-7040.

I hereby certify that this correspondence is facsimile transmitted to the Commissioner for Patents, Alexandria, VA 22313-1450, at (703) 872-9306, on February 19, 2004.

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February 19, 2004
Date of Signature

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